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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/455,486	12/06/1999	DANIEL E. AFAR	1703-011.US2	5189

7590 03/04/2004

Kate H. Murashige
Morrison & Foerster LLP
3811 Valley Centre Drive Suite 500
San Diego, CA 92130

EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/455,486	AFAR ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 44-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 44-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Request for Continued Examination

The request filed on 12/31/2003 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/455486 is acceptable and a RCE has been established. An action on the RCE follows.

Claims 1, and 44-48 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 1, and 44-48 remain rejected under 35 USC 112, 1st paragraph for the reasons of record (see Advisory Action mailed 10/02/03 and Final Rejection mailed 1/29/03). The claims are drawn to an isolated polypeptide (SEQ ID NO:6, termed "STEAP-2") and compositions and kits thereof. It has been maintained throughout the prosecution of this application that the disclosure as a whole (including the specification, art of record, and inventor's declarations) failed to provide sufficient guidance and objective evidence that lends reasonability predictability to the use (and thus enablement) of the claimed polypeptide. The original basis of this rejection (Non-Final Rejection, mailed 4/12/2001) was non-enablement of a cancer treatment using a vaccine comprising a STEAP-2 protein and the unpredictability of the use of the protein for diagnosing cancer. The later issue has become central to the prosecution of this case with the Office taking the position that, those of skill in the art recognize that expression of mRNA,

specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression.

It is noted that four declarations have been filed in this application's history. Two by Dr. Mary Faris (June 2002 and August 2003), one by Dr. Karen Morrison (August 2003), and one by Dr. Pia Challita-Eid (February 2004). Since the August 2003 declarations have been previously considered (Advisory Action, mailed 10/02/03), they will not be further considered on the merits. Applicants further request (Remarks, 12/31/2003, page 2) that the declaration executed by Dr. Faris in June 2002 be considered with this now filed RCE. However, it should be noted that the Faris declaration of June 2002 was *previously* considered as so evidenced by the Advisory Action mailed 08/20/2002. However, to facilitate compact prosecution, the Faris Declaration of June 2002 will only be re-visited, in-part, because much of the content had been re-presented in Dr. Faris's second declaration.

It is noted that applicant's have filed a new Declaration by Dr. Pia Challita-Eid, Ph.D filed February 17, 2004 that accompanies the filing of an RCE. The Declaration appears to support the diagnostic use, and thus enablement of the STEAP-2 *polynucleotide*, wherein there is a predictive difference between measuring the relative abundance of the polynucleotide in cancerous samples versus normal samples (Exhibits 2 & 3). The Declaration also appears to teach that the STEAP-2 polypeptide is expressed and detected via antibodies specific for the STEAP-2 polypeptide in prostate cancer and lung cancer (Exhibit 7). Dr. Challita-Eid argues that (page 4, item 10) the STEAP-2 protein is expressed in cells, and that it is a useful marker for cancer tissues. Further, the Faris declaration (June 2002) illustrates that PC-3 cells and 3T3 cells, which were modified to contain an expression system for STEAP-2, showed enhanced levels of

tyrosine phosphorylation and that *in-vitro* translation studies using rabbit reticulocyte lysate, show that the STEAP-2 protein is translated and exhibits the expected molecular weight.

These declarations have been carefully considered but are not found persuasive for the reasons of record. As set forth previously, those of skill in the art, recognize that expression of mRNA, specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. There are many steps in the pathway leading from DNA to protein, and all of them can in principle be regulated. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465- attachment mailed 04/12/2001) illustrate post-transcriptional regulation of ferritin wherein the translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferin receptor polypeptide is translated. Lewin, B. also teaches (Genes VI, Oxford University Press, Inc., NY, Chapter 29, 1997) that a major control point for genes exists during the initiation of transcription by the interaction of the RNA polymerase with its promoter. Concurring with Alberts *et al.*, Lewin further acknowledges downstream control of gene expression since translation of mRNA in the cytoplasm is also a point of control. Also, with regards to tumor associated antigens, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401, attachment mailed 04/12/2001) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Furthermore, Rama *et al.* (Biochem. J. Vol. 318, 1996, pages 333-341) teach that the glucocorticoid, betamethasone, increased mRNA expression of cholinephosphate cytidylyltransferase (CT) as determined by RT-PCR and Southern analysis, but did not alter the levels of the CT enzyme as assayed by Western blotting

(abstract, and page 339, 2nd column, 2nd paragraph). Finally, Lewin acknowledges that control of gene expression can occur at multiple stages and that production of RNA cannot inevitable be equated with production of protein. Thus, the predictability of protein translation and its possible utility as a diagnostic are not necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Furthermore, if a molecule such as STEAP-2 is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins, including STEAP-2, are expressed in normal tissues and diseased tissues as so evidenced by the disclosure (page 12, lines 9-10). Therefore, one needs to know, e.g., that the claimed polypeptide is present only in cancer tissue to the exclusion of normal tissue. Thus, in the absence of any correlation between the claimed encoded antigen with any known disease or disorder, any information obtained from various expression profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself. Therefore, absent evidence of the protein's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the antigen in any diagnostic setting without undue experimentation. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

No claim is allowed.

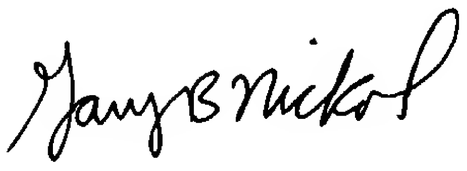
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN



GARY NICKOL
PRIMARY EXAMINER